Application No.: 10/084,380 -2 - Docket No.: 20555/0203244-US0

## AMENDMENTS TO THE SPECIFICATION

Please amend paragraph [0063] that bridges pages 15-16 to read as follows:

[0063] Without being limited, the method of detecting provides an antibody molecule which is free end-specific for the N-terminus or the C-terminus of an amyloid  $\beta$  peptide and/or fragments thereof namely, the 'spanning peptide ELISA detection method' is as follows: antibodies that bind sequences in the N-terminus region of amyloid β peptide, (for example residues 1-5 of Peptide A or Asp-Ala-Glu-Phe-Arg (SEQ ID NO: 14); see Figure 4), and also bind the identical sequence of amino acids in the spanning peptide C, which corresponds to sequences of the amyloid precursor protein (APP), are eliminated from the screen. Only antibodies that bind (NH<sub>2</sub>)Asp-Ala-Glu-Phe-Arg (SEQ ID NO: 14) with a free N-terminus (for example, the heptamer peptide or full length A\beta 1-40), but do not bind the spanning peptide, are selected in this detection system. These selected antibodies should be described as 'free N-end-specific' because their binding epitope incorporates both a high affinity recognition element for a free amino (NH<sub>2</sub>) group, in addition to recognition of the N-terminal amino acid residues of the particular amyloid-β peptide. A similar detection system is envisaged for selecting antibodies that are C-end-specific using a spanning peptide that corresponds to a contiguous sequence of amino acids on both sides of the Cterminal cleavage sites in APP. This exquisite sensitivity of free-end specific antibodies is required so as not to affect the normal biological functions of the transmembrane receptor-like APP molecule that is implicated in several important physiological roles (such as mediation in adhesion, growth promoting effects, neuroprotection, neuritic outgrowth, recycling of synaptic vesicles, regulation of apoptosis inhibition of serine proteases, receptor and signal transduction functions, calcium metabolism and nucleic acid transcription). Thus, in one embodiment, the invention utilizes freeend specific antibodies to inhibit the accumulation of amyloid β peptides, to ameliorate or prevent the neurotoxic consequences of amyloid deposition, to slow Alzheimer's Disease or other diseases characterized by amyloid β deposition progression or to delay their onset.

Please amend paragraph [0073] that appears on page 18 to read as follows:

• [0073] H<sub>2</sub>N-Asp-Ala-Glu-Phe-Arg-His-Asp-Ser-Gly-Tyr-Glu-Val-His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-Glu-Asp-Val-Gly-Ser-Asn-Lys-Gly-Ala-Ile-Ile-Gly- Leu-Met-Val-Gly-Gly-Val-Val-Ile-Ala-OH (SEQ ID NO: 15).

Please amend paragraph [0102] that bridges pages 27-28 to read as follows:

NO: 16) was conjugated to BSA through a SMCC linker. Swiss Webster mice were immunized with 100  $\mu$ g of this conjugate in Freund's complete adjuvant and then boosted twice with a further 100  $\mu$ g of conjugate in Freund's incomplete adjuvant. Antisera were screened using the 'spanning peptide ELISA detection method', as described in the specification. Briefly, A $\beta$ 1-40 was coated onto 96-well plates, which were then incubated with samples in the presence of competing peptides A (immunogen), C (spanning peptide), or A $\beta$ 1-40 itself. The common result is shown in Figure 5. As expected, antibodies produced by these animals bind residues 1-5 of A $\beta$  (peptide A), which was the peptide used for immunization, and the full-length A $\beta$ 1-40 peptide. However, these antibodies are also reactive with the A $\beta$ 1-5 epitope when flanked by additional sequences on its N-terminus (peptide C), as is the case in the intact amyloid precursor protein APP. Such antibodies may be referred to as epitope-specific (for sequences 1-5 of the N-terminus of A $\beta$ ).

Please amend paragraph [0104] that appears on page 18 to read as follows:

[0104] Peptide H<sub>2</sub>N-Asp-Ala-Glu-Phe-Arg-His-aminohexanoate-Cys-amide (SEQ ID NO: 16) was conjugated to KLH through an MBS linker Balb/c x C57B1/6 F1 mice were am immunized with 50 μg of this conjugate in Freund's complete adjuvant and then boosted four times with a further 50 μg of conjugate in Freund's incomplete adjuvant. Antisera were tested and fusions performed using standard methods. Hybridomas were screened using the 'spanning peptide ELISA detection method', as described in the specification. Briefly, either positive peptide (H<sub>2</sub>N-Asp-Ala-Glu-Phe-Arg-His (SEQ ID NO: 6) conjugated to BSA) or negative control 'spanning' peptide (acetyl-Glu-Val-Lys-Met-Asp-Ala-Glu-Phe-Arg-His) (SEQ ID NO: 17) were coated onto

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96-well plates, which were then incubated with hybridoma supernatants. As seen in Figures 7 and 8, some hybridomas recognize both peptides in a similar manner (i.e. clones 5E2, 2A8, and 2F8) or with insignificant differences (i.e. clones 4H9, 1C12, and 3H3). However, some clones demonstrate free-end specificity in that they recognize the positive peptide used for immunization much greater than they recognize the negative control spanning peptide, which in fact contains the same sequence used for immunization. Examples are seen in clones 4D12 and 2A10 of this fusion.